(b) the cell is a germ cell which gives rise to progeny ectodermal cells and the method further comprises the step of detecting the functional expression of the TAJ gene or gene product in the progeny cells.

REMARKS

Amendments

The specification is amended to correct two minor typos: the roman numeral designation for the sixth example and the spelling of "cell". The independent claims 1 and 9 are restricted to human TAG gene and gene product, which is the principally exemplified species (e.g. p.3, lines 17-18; p.5, lines 1-2; p.12, line 26; p.14, line 21; p.23, line 13, etc.); claim 9 is further amended to grammatically clarify the detecting step; and dependent claims have been prefaced with the definite article "the", as requested. These amendments introduce no new matter.

35USC112, second paragraph

As amended, the claims require detecting (or modulating the functional expression of) a *human* TAJ gene or gene product. The murine and human TAJ genes and corresponding gene products are known in the art (Specification, p.1, lines 21-22). Furthermore, the present specification expressly recites the nucleotide and amino acid sequences of the full-length human TAJ protein and its native coding sequence (SEQ ID NOS:2 and 1, respectively). As explained in the specification, mutations in the TAJ gene, particularly mutations causing truncated TAJ proteins, are associated with disease (Specification p.3, lines 1-6). The human TAJ gene or gene product subject to detection or modulation may be a mutation of the disclosed wild-type TAJ sequence (Specification p.3, line 16 - p. 4, line 3), and it is the disclosed wild-type sequences that are used to detect or modulate such mutants (Specification p.4, line 31 - p.6, line 2; p.7, line 21 - p.8, line 18; see also Examples IV, V and VI). Accordingly, what is a "human TAJ gene or gene product" is clearly defined to those skilled in the art.

Though there is no evidence to the contrary, we provide herewith an expert Declaration under 37CFR1.132 documenting that the claims are definite to those of ordinary skill in the art, and that the specification provides such practitioners a clear understanding of what is

encompassed by the recitation of "a human TAJ gene or gene product".

The suggested article amendment of claims 2-8 and 10-21 has been made.

35USC112, first paragraph (written description)

As amended, the claims require detecting (or modulating the functional expression of) a human TAJ gene or gene product. The murine and human TAJ genes and corresponding gene products are known in the art (Specification, p.1, lines 21-22). Furthermore, the present specification expressly recites the nucleotide and amino acid sequences of the full-length human TAJ protein and its native coding sequence (SEQ ID NOS:2 and 1, respectively). As explained in the specification, mutations in the TAJ gene, particularly mutations causing truncated TAJ proteins, are associated with disease (Specification p.3, lines 1-6). Hence, the human TAJ gene or gene product subject to detection or modulation may be a mutation of the disclosed wild-type TAJ sequence (Specification p.3, line 16 - p. 4, line 3). However, it is the disclosed wild-type sequences that are used to detect or modulate such mutants (Specification p.4, line 31 - p.6, line 2; p.7, line 21 - p.8, line 18; see also Examples IV, V and VI). Accordingly, the steps of the claimed method are clearly described in the specification to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Though there is no evidence to the contrary, we provide herewith an expert Declaration under 37CFR1.132 documenting that the claimed subject matter is described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention, particularly the claimed methods for detecting (or modulating the functional expression of) a human TAJ gene or gene product.

35USC112, first paragraph (enablement)

As amended, the claims require detecting (or modulating the functional expression of) a human TAJ gene or gene product. In particular, the TAJ detecting claims, as claim 1, require (a) detecting the presence of a human TAJ gene or gene product in a cell; and (b) correlating the

presence of the TAJ gene or gene product with a presence of or predisposition to an ectodermal disorder.

The specification thoroughly teaches and exemplifies the method defined by these steps, readily enabling one of ordinary skill in the art to practice the method as claimed without undue experimentation. For step (a), the specification describes a variety of suitable detection methodologies (p.4, lines 9-28; p.6, lines 3-13), teaches a large panel of exemplary TAJ specific probes (allele-specific antibodies and hybridization probes; p.4, line 31 - p.6, line 2), and provides detailed exemplification of detection by in situ and chromosomal hybridization (p.9, lines 3-17), TAJ allele-specific PCR amplification (p.12, lines 5-22), transcriptional reporter assay (p.10, lines 6-29), and immunocytochemistry (p.14, line 29 - p.15, line 5); see also p.17, lines 14-31. Step (b) involves no more than correlating the detected TAJ gene or gene product with an ectodermal disorder. In many cases, this entails no more than cross-referencing to a known clinical correlate. The specification describes alternative means to implement this step (p.6, lines 14-26), teaches a large panel of TAJ genes and gene products associated with an ectodermal disorder (p.3, line 16 - p.4, line 3) and provides detailed exemplification of correlation by chromosomal mapping (p.9, lines 12-17), animal model (p.9, line 18 - p.10, line 3) and clinical diagnosis (p.12, lines 5-22).

Both required steps of these TAJ detecting claims are thoroughly taught, described and exemplified, fully enabling one skilled in the art to practice the claimed invention without undue experimentation. The Action's criticisms of the data reported in the application, and particularly the reporting of qualitative as opposed to quantitative data, are believed to reside outside the bounds of a proper enablement analysis duly limited to the recited claims. Though there is no evidence to the contrary, we provide herewith an expert Declaration under 37CFR1.132 documenting that the specification readily enables one of ordinary skill in the art to practice this two-step detection method as claimed without undue experimentation.

As amended, the TAJ modulating claims require contacting a cell with an agent which specifically binds and modulates the functional expression of a human TAJ gene or gene product, wherein (a) the cell is an ectodermal cell; or (b) the cell is a germ cell which gives rise to progeny ectodermal cells and further detecting the functional expression of the TAJ gene or gene product

in the progeny cells.

The specification thoroughly teaches and exemplifies the method defined by these steps, readily enabling one of ordinary skill in the art to practice the method as claimed without undue experimentation. The specification explains how this method is implemented, including its application to germ cells which give rise to progeny ectodermal cells (p.6, line 29 - p.7, line 9), describes a variety of suitable TAJ binding and modulatory agents (p.7, lines 10-19), teaches a panel of exemplary agents shown to allele-specifically modulate functional expression of a TAJ gene or gene product (p.7, line 21 - p.8, line 18), describes how these agents are delivered to the cell (p.8, lines 20-30), and provides detailed exemplification of the method as applied to human keratinocytes in vitro and in vivo (Examples V and VI, p.12, line 24 - p.17, line 31).

The required step(s) of the TAJ modulating claims are thoroughly taught, described and exemplified, fully enabling one skilled in the art to practice the claimed invention without undue experimentation. The Action's criticisms of the data reported in the application, and particularly the reporting of qualitative as opposed to quantitative data, are believed to reside outside the bounds of a proper enablement analysis duly limited to the recited claims. The Action's suggestion that correlating the many ectodermal disorders that may be associated with TAJ mutations would involve undue trial and error appears to read much too much into the required claim step. Our claims do not require correlating every ectodermal dysplasia with every TAJ mutation, but merely detecting *a* TAJ mutant and then correlating *that* mutant to the presence of *an* ectodermal disorder. Note, for example, the exemplification shown in Example IV (p.12, lines 5-22). There is no trial and error – the cell comes from a particular source (e.g. patient) having a particular clinical presentation, to which the practitioner is not blind. In fact, a particular clinical presentation of ectodermal disease is the reason the patient's TAJ gene is being analyzed. In *In re Wands*, the enablement issue was not whether it would require undue experimentation to make all the possible antibodies having the required affinity, but rather whether it would require undue experimentation to make a given such antibody. Similarly, here the issue is not whether it would require undue experimentation to analyze the correlation of every possible TAJ mutant with every possible ectodermal disorder, but rather whether it would require undue experimentation to analyze the correlation of *a* TAJ mutant to *an* ectodermal

disorder - and one single disorder will suffice for our claims.

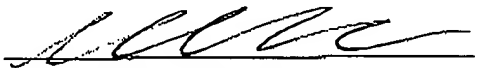
Though there is no evidence to the contrary, we provide herewith an expert Declaration under 37CFR1.132 documenting that the specification readily enables one of ordinary skill in the art to practice this modulation method as claimed without undue experimentation.

Aspects of this invention were published by Eby et al, J Biol Chem. 2000 May19;275(20):15336-42.

The Examiner is invited to call the undersigned if he would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

Applicants hereby petition for any necessary extension of time pursuant to 37 CFR 1.136(a). The Commissioner is hereby authorized to charge any fees or credit any overcharges relating to this communication to our Deposit Account No. 19-0750 (order no. UTSD:0680).

Respectfully submitted,
SCIENCE & TECHNOLOGY LAW GROUP



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